510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K061687

B. Purpose for Submission:

Confirmatory testing for extended spectrum Beta- lactamase (ESBL) in *Escherichia coli, Klebsiella oxytoca, K. pneumonia,* and *Proteus mirabilis.*

C. Measurand:

ESBL confirmation with: Ceftazidime (1, 8 µg/mL), Ceftazidime/clavulanic acid (0.25/4, 2/4 µg/mL), and Cefotaxime 2, 16 µg/mL), Cefotaxime/clavulanic acid (0.5/4, 4/4 µg/mL)

D. Type of Test:

Qualitative growth based detection

E. Applicant:

Dade Behring
Dade MicroScan Inc.

F. Proprietary and Established Names:

MicroScan® Dried Gram-Negative MIC/Combo Panels

G. Regulatory Information:

1. Regulation section:
   866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:
   Class II

3. Product code:
   JWY - Manual Antimicrobial Susceptibility Test Systems
   LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems
   LTT – Panels, Test, Susceptibility, Antimicrobial

4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):

   ESBL confirmation with Ceftazidime (1, 8 µg/mL), Ceftazidime/clavulanic acid (0.25/4, 2/4 µg/mL), and Cefotaxime 2, 16 µg/mL), Cefotaxime/clavulanic acid (0.5/4, 4/4 µg/mL) for use with MicroScan® Dried Gram Negative MIC Combo Panels and Dried Gram Negative Breakpoint Combo Panels. MicroScan® panels are designed for use in determining antimicrobial agent susceptibility and/or identification to the species level of aerobic and facultatively anaerobic gram negative bacilli.

2. Indication(s) for use:

   The MicroScan® Dried Panels containing ceftazidime/clavulanic acid and cefotaxime/clavulanic acid can be used to confirm the presence of ESBLs production in *Escherichia coli*, *Klebsiella oxytoca*, *Klebsiella pneumonia*, and *Proteus mirabilis.*

3. Special conditions for use statement(s):
   The Prompt® method of inoculation is an alternate method of inoculation preparation that is supported in the methodology along with the turbidity method. The stationary and log inoculum methods should not be used with this antibiotic.

4. Special instrument requirements:

   Readings may be performed on the autoSCAN®-4 and WalkAway® Systems.

I. Device Description:

This submission is for the AST Panel only. The ID System was not reviewed.
The MicroScan® Dried Gram-Negative MIC/Combo Panel contains microdilutions of each antimicrobial agent in various concentrations with Mueller Hinton Broth and various nutrients which are dehydrated and dried in panels. Each panel contains two control wells: a no-growth control well (contains water only/no nutrients or broth), and a growth control well (contains test medium without antibiotic). The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum prepared in water, then 0.1ml transferred to 25ml of inoculum water containing pluronic-D/F-a wetting solution) for a final inoculum of 3-7 X 10^5. The Prompt® method of inoculation is also recommended as an alternate means of preparing the inoculum. The panels are incubated at 35^o C in a non-CO_2 incubator for 16-20 hours and read by visual observation of growth. Panels may be

read manually, with the autoSCAN®-4 or WalkAway® Systems.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   MicroScan Dried Gram-Negative MIC/Combo Panels

2. Predicate 510(k) number(s):

   K020037 ESBL confirmation

1. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	MicroScan® Dried Gram-Negative MIC panels for confirmation of ESBL	Same
Inoculum preparation	Inoculum prepared from isolated colonies using either the Turbidity method or Prompt® system	Same
Technology	Growth based after 16 hours incubation	Same
Results	Confirmed ESBL producers report as resistant for all penicillins, cephalosporins and aztreonam	Same
Differences		
Item	**Device**	**Predicate**
Test organism	*Escherichia coli, Klebsiella pneumonia, K. oxytoca,* and *Proteus mirabilis*	*Escherichia coli, Klebsiella pneumonia, and K. oxytoca*
Antibiotic	Cefotaxime (2, 16 µg/mL) Cefotaxime.clavulanic acid (0.5/4, 4/4 µg/mL) Ceftazidime (1,8 µg/mL) Ceftazidime/clavulanic acid (0.25/4, 2/4 µg/mL)	Cefotaxime and Ceftazidime (0.5-128 µg/mL), Ceftazidime/clavulanic acid and Cefotaxime/clavulanic acid (0.12/4-32/4 µg/mL)

K. Standard/Guidance Document Referenced (if applicable):

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA"; CLSI M7 (M100-S16) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically;

Approved Standard".

L. Test Principle:

After incubation in a non-CO_2 incubator for 16-20 hours, the minimum inhibitory concentration (MIC) for the test organisms are read by determining the lowest antimicrobial concentration showing inhibition of growth. The panels can be read manually and with the autoSCAN®-4 by observing growth or no growth or with the use of the WalkAway® instrument, which uses an optics system with growth algorithms to directly measure organism growth.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was demonstrated using 12 isolates of *P. mirabilis E. coli and Klebsiella spp.* tested at 3 sites on 3 separate days in triplicate. The study included the testing of both the turbidity inoculum method and Prompt® method of inoculation with readings performed manually, with the autoSCAN®-4 and WalkAway® Systems. All methods provided acceptable reproducibility.

b. Linearity/assay reportable range:

Not Applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Quality Control with *E. coli* ATCC 25922 and *K. pneumoniae* ATCC 700603 were tested with the expected result on most days using the Prompt® and the turbidity method of inoculation with readings performed manually, with the autoSCAN®-4 and WalkAway® Systems. The Prompt® failed Quality control on slightly more occasions than the turbidity method of inoculation but still provided acceptable results overall. The method of reading made no difference in the results.

Inoculum density control: A turbidity meter was used for the turbidity inoculation method with daily checks. The Prompt® method of inoculation had colony counts performed periodically throughout the study to determine the average inoculum density since there is no visual check of the inoculum using this device. The average of the Quality Control recommended isolates were acceptable except an occasional colony count outside the recommended range for the CLSI reference method.

d. Detection limit:

Not Applicable

e. Analytical specificity:

Not Applicable

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

A total of 95 isolates of *P. mirabilis, E. coli*, and *K. oxytoca* and *K. pneumonia* that were previously molecular characterized were tested at one site. Forty two of these were ESBL positive. These 95 were tested with both the Prompt® and the turbidity methods of inoculation. Data was analyzed using the streamlined dilutions of Ceftazidime (1, 8 µg/mL), Ceftazidime/clavulanic acid (0.25/4, 2/4 µg/mL), and Cefotaxime 2, 16 µg/mL), Cefotaxime/clavulanic acid (0.5/4, 4/4 µg/mL) and compared to the expected molecular result. Results were exactly the same no matter which read method was used with the turbidity method of inoculation (see chart below for % agreement) The Prompt® method of inoculation had more variability with both one additional false positive with the manual read method and 2 false positives with the instrument read results. The following charts demonstrates the performance as compared to molecular characterization using the turbidity and the Prompt® methods of inoculation with results read manually and with the AutoSCAN®- 4 and WalkAway® Systems.

Turbidity Method of Inoculation

Organism	Read Method					
	MANUAL		WALKAWAY		autoSCAN-4	
	ESBL +	ESBL -	ESBL +	ESBL -	ESBL +	ESBL -
E. coli	11/13*	13/13	11/13	13/13	11/13	13/13
K. spp.	16/16	18/18	16/16	18/18	16/16	18/18
P. mirabilis	12/13*	22/22	12/13	22/22	12/13	22/22
TOTAL	39/42	53/53	39/42	53/53	39/42	53/53
% agreement with expected (95% CI)	93% (80.5-98.5)	100% (93.3 - 100)	93% (80.5-98.5)	100% (93.3 - 100)	93% (80.5-98.5)	100% (93.3 - 100)

Prompt® Method of Inoculation

Organism	Read Method					
	MANUAL		WALKAWAY		autoSCAN-4	
	ESBL +	ESBL -	ESBL +	ESBL -	ESBL +	ESBL -
E. coli	12/13*	12/13	12/13	11/13	12/13	11/13
K. spp.	16/16	18/18	16/16	18/18	16/16	18/18
P. mirabilis	12/13*	22/22	12/13	22/22	12/13	22/22
TOTAL	40/42	52/53	40/42	51/53	40/42	51/53
% Agreement with expected (95% CI)	95% (83.8-99.4)	98% (89.9-100)	95% (83.8-99.4)	96% (87.0-99.6)	95% (83.8-99.4)	96% (87.0-99.6)

*One *E. coli* and one *P. mirabilis* were false negative when compared to the molecular characterized expected result. These were also falsely negative when testing was performed as recommended by the CLSI reference method.

b. Matrix comparison:

Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical specificity:

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

Quality Control values and recommendations are included in the package insert.

N. Proposed Labeling:

Quality Control testing is the same as recommended in the reference method

described by CLSI and is included in the package insert.

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.